JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY

Origin and Mechanistic Pathways of Formation of the Parent Furan—A Food Toxicant

CAROLINA PEREZ LOCAS AND VAROUJAN A. YAYLAYAN*

Department of Food Science and Agricultural Chemistry, McGill University, 21, 111 Lakeshore, Ste. Anne de Bellevue, Quebec, Canada H9X 3V9

Studies performed on model systems using pyrolysis−GC-MS analysis and ^{13}C-labeled sugars and amino acids in addition to ascorbic acid have indicated that certain amino acids such as serine and cysteine can degrade and produce acetaldehyde and glycolaldehyde that can undergo aldol condensation to produce furan after cyclization and dehydration steps. Other amino acids such as aspartic acid, threonine, and α-alanine can degrade and produce only acetaldehyde and thus need sugars as a source of glycolaldehyde to generate furan. On the other hand, monosaccharides are also known to undergo degradation to produce both acetaldehyde and glycolaldehyde; however, ^{13}C-labeling studies have revealed that hexoses in general will mainly degrade into the following aldotetrose derivatives to produce the parent furan—aldotetrose itself, incorporating the C3−C4−C5−C6 carbon chain of glucose (70%); 2-deoxy-3-ketoaldotetrose; incorporating the C1−C2−C3−C4 carbon chain of glucose (15%); and 2-deoxyaldotetrose, incorporating the C2−C3−C4−C5 carbon chain of glucose (15%). Furthermore, it was also proposed that under nonoxidative conditions of pyrolysis, ascorbic acid can generate the 2-deoxyaldotetrose moiety, a direct precursor of the parent furan. In addition, 4-hydroxy-2-butenal—a known decomposition product of lipid peroxidation—was proposed as a precursor of furan originating from polyunsaturated fatty acids. Among the model systems studied, ascorbic acid had the highest potential to produce furan, followed by glycolaldehyde/alanine > erythrose > ribose/serine > sucrose/serine > fructose/serine > glucose/cysteine.

KEYWORDS: Monosaccharides; serine; cysteine; alanine; ascorbic acid; 4-hydroxy-2-butenal; lipid peroxidation; mechanisms of formation of furan; ^{13}C-labeled glucose and serine; Py-GC-MS analysis

INTRODUCTION

Recently, researchers at the U.S. Food and Drug Administration (*1*) have identified the parent compound furan in a number of foods that undergo thermal treatment, especially canned and jarred foods. Furan is a volatile and colorless liquid and is classified as a possible human carcinogen by the International Agency for Research on Cancer (IARC) (*2*). Although the parent furan had previously been reported in various foods such as coffee, canned meat, baked bread, and cooked chicken (*3*−*5*), it was only recently that a more comprehensive study was performed by the FDA using larger number of food samples, which found furan levels ranging up to ∼100 ppb.

According to Maga (*3*) the primary source of furans in food is thermal degradation of carbohydrates such as glucose, lactose, and fructose. According to the FDA, a variety of carbohydrate/amino acid mixtures or protein model systems (e.g., alanine, cysteine, casein) and vitamins (ascorbic acid, dehydroascorbic acid, thiamin) have been used to generate furans in food. Furthermore, Health Canada (*6*) reported the formation of furan from ascorbic acid and from the oxidation of polyunsaturated fatty acids (PUFA). The latter finding, however, should not come as a surprise because a furan derivative, 5-pentylfuran, has already been detected in oxidized soybean oil (*7*) and is used currently as a chemical marker for rancidity. The origin of 5-pentylfuran was linked to the formation of 4-hydroxy-2-nonenal (4-HNE) by Sayre et al. (*8*) when they observed the formation of the furan upon refluxing ethanolic solution of 4-HNE under acidic conditions. This observation was later confirmed by Erdelmeier et al. (*9*). Recent studies found a significant correlation between 5-pentylfuran concentrations with the time of oxidation of olive oil (*10*).

In general, the oxidative degradation of PUFAs and the formation of lipid peroxides are known to play a major role in the development of both degenerative diseases in biological systems (*11*) and off-flavors and rancidity in food systems (*10*). Lipid hydroperoxides can be formed from PUFA nonenzymatically by reactive oxygen species or enzymatically by lipoxygenases. Subsequent homolytic cleavages of PUFA hydroperoxides, catalyzed by transition metal ions, result in the formation of 2-alkenals, 4-oxo-2-alkenals, and 4-hydroxy-2-alkenals (*11*) (see **Figure 1**). Highly cytotoxic 4-hydroxy-2-alkenals such as 4-HNE are capable of the modification of proteins, DNA, and low-density lipoprotein (LDL).

* Corresponding author [telephone (514) 398-7918; fax (514) 398-7977; e-mail varoujan.yaylayan@mcgill.ca].

10.1021/jf0490403 CCC: $27.50
Published on Web 10/12/2004

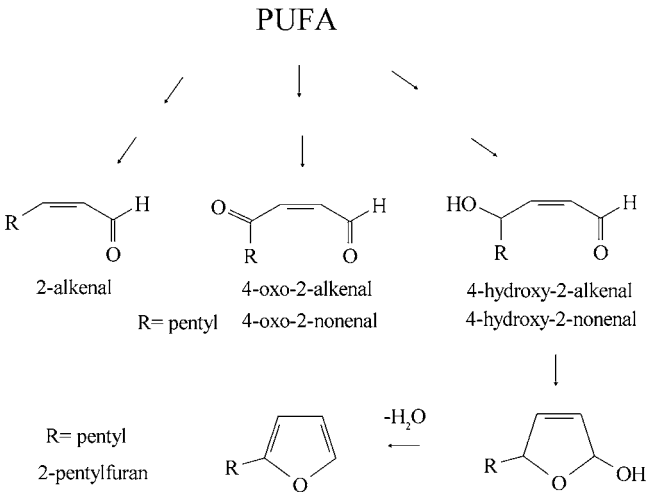

Figure 1. Summary of different reactive aldehydes formed from oxidative decomposition of polyunsaturated fatty acids (PUFA).

On the basis of the above discussion, it can be proposed that the parent furan, similar to 5-pentylfuran, could be formed from corresponding 4-hydroxy-2-butenal (*12*) through cyclization and formation of 2,5-dihydro-2-furanol and subsequent dehydration as proposed in **Figure 2**. Ironically, this process converts the more toxic 4-hydroxy-2-alkenals into less toxic and more volatile furan derivatives. At present, there are no specific mechanisms proposed that can explain the formation of the parent furan from other sources such as carbohydrates and amino acids. In this study we provide evidence for the mechanism of formation of the parent furan from amino acids, sugars, amino acid/sugar mixtures, and ascorbic acid.

MATERIALS AND METHODS

All reagents and chemicals were purchased from Aldrich Chemical Co. (Milwaukee, WI) and used without further purification. The labeled [^{13}C-1]serine (99 atom %) [^{13}C-2]serine, and [^{13}C-3]serine (99 atom %) and the labeled D-[1-^{13}C]glucose (99 atom %), D-[2-^{13}C]glucose (99 atom %), and D-[6-^{13}C]glucose were also purchased from Aldrich Chemical Co. D-[3-^{13}C]Glucose (99 atom %), D-[4-^{13}C]glucose (99 atom %), and D-[5-^{13}C]glucose (99 atom %) were purchased from Cambridge Isotope Laboratories (Andover, MA).

Pyrolysis−GC-MS Analysis. *Mechanistic Studies.* All Py-GC-MS analyses were performed using a Hewlett-Packard 5890 series II GC fitted with a 5971B MS (Hewlett-Packard, Palo Alto, CA) and a CDS Pyroprobe 2000 interface (CDS Analytical Inc., Oxford, PA). Single compounds or binary mixtures of D-glucose/ amino acid (1:1 molar ratio, total 2 mg), except for labeling studies performed with D-glucose/ L-serine (1:3 molar ratio, total 2 mg), were introduced inside a quartz tube (0.3 mm thickness), plugged with quartz wool and inserted into the coil probe. The pyroprobe was set at 250 °C at a heating rate of 50 °C/s with a total heating time of 20 s. The pyroprobe interface was set at 250 °C. The samples were introduced in splitless mode and analyzed under a constant He flow of 1.34 mL/min, the pressure being regulated by an electronic pressure controller (Hewlett-Packard). The capillary direct MS interface temperature was 180 °C; the ion source was 280 °C. The ionization voltage was 70 eV and the electron multiplier, 2047 V. The MS scanned masses from *m*/*z* 17 to 500 at 1.5 scans/s; the column temperature (PLOT-Q capillary column from Hewlett-Packard, Mississagua, ON) was held at 40 °C for 2 min, then increased to 100 °C at a rate of 30 °C/min, and further increased to 250 °C at a rate of 10 °C/min and kept at 250 °C for 10 min. Compounds were tentatively identified by comparing their mass spectra with those of Wiley and NIST mass spectral databases. The identity and purity of the chromatographic peaks were determined using NIST AMDIS version 2.1 software.

Efficiency of Furan Formation. Single compounds (7 μmol) listed in **Table 1** were mixed with silica gel (1 mg) except ascorbic acid

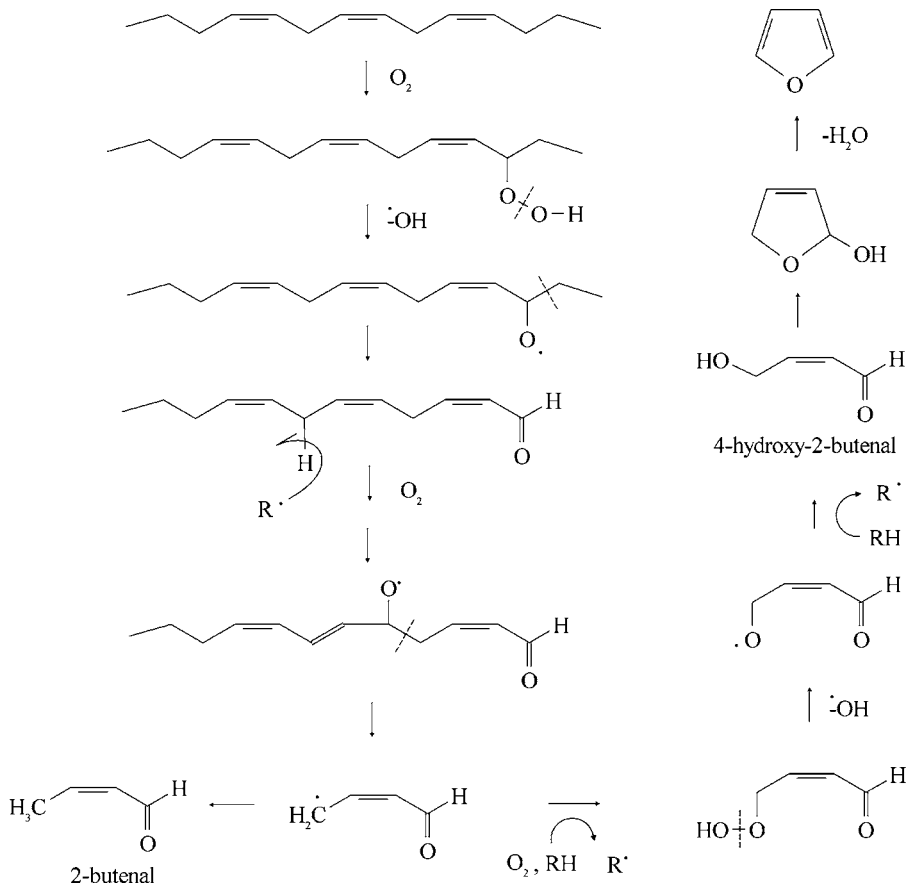

Figure 2. Proposed mechanism of lipid peroxidation and subsequent formation of furan.

Table 1. Relative Efficiency of Furan Formation Expressed as Area Count of Furan per Mole of Starting Material Generated from Different Model Systems at 250 °C

model system	rel efficiency × 10^{10} (area/mol)
L-ascorbic acid	140
dehydroascorbic acid[a]	78
dehydroascorbic acid[b]	47
D-erythrose	32
dehydroascorbic acid	8
D-ribose	7
D-sucrose	5
D-glucose	4
D-fructose	4
L-serine	1
L-cysteine	0.5
L-threonine	0
L-aspartic acid	0
L-alanine	0
L-glycine	0
D-ribose/serine	28
D-sucrose/serine	24
D-fructose/serine	16
D-glucose/cysteine	15
D-glucose/serine	11
D-glucose/alanine	10
D-glucose/L-aspartic acid	9
D-glucose/formate sodium	9
D-glucose/L-threonine	5
D-glucose/glycine	5
D-erythrose/L-serine	3
glycolaldehyde[c]/L-alanine	65
glycolaldehyde[c]/L-serine	9
acetaldehyde[d]/glycolaldehyde[c]	7
acetaldehyde[d]/L-serine	0.5
L-serine/L-alanine	0.4

[a] Pyrolysis temperature = 350 °C. [b] Pyrolysis temperature = 300 °C. [c] From glycolaldehyde dimer. [d] From acetaldehyde diethyl acetal.

(reacted without silica gel) and were pyrolyzed as indicated above at 250 °C unless otherwise specified. All pyrolyzed model systems contained 7 μmol of each reagent indicated except in the case of sodium formate, which was 10 μmol. The reported formation efficiency values are the average of duplicate analyses and are rounded off, with no more than 6% relative error in reproducibility.

RESULTS AND DISCUSSION

Numerous derivatives of the parent compound furan such as 5-methylfurfural, furanmethanol, 2-acetylfuran, 2-methyldihydro-3(2*H*)-furanone, and 4-hydroxy-2,5-dimethyl-3(2*H*)-furanone have been characterized in Maillard model systems and their mechanisms of formation identified using ^{13}C-labeled sugars (*13*, *14*). In these studies, the parent furan was not detected because the common gas chromatographic columns employed during such studies were more polar DB-5 type columns rather than the required less polar columns such as PLOT that are able to retain gaseous and nonpolar compounds such as the parent furan. Although we had previously analyzed serine (*15*) and cysteine (*16*) model systems on a PLOT-Q column and observed the formation of the parent furan, we have not reported its formation mechanism. In this study, we investigated in detail the formation of furan from different sugars and amino acid model systems, including ascorbic acid, using Py-GC-MS. **Table 1** summarizes the efficiency of different model systems to produce furan under identical conditions expressed as furan peak area per mole of starting material, and **Figure 3** summarizes the general pathways leading to furan formation starting from carbohydrates and amino acids, and including PUFA.

Furan Formation through Amino Acid Degradation. Previous studies (*16*) using a PLOT-Q column have indicated the formation of the parent furan in model systems containing serine and cysteine, even in the absence of reducing sugars

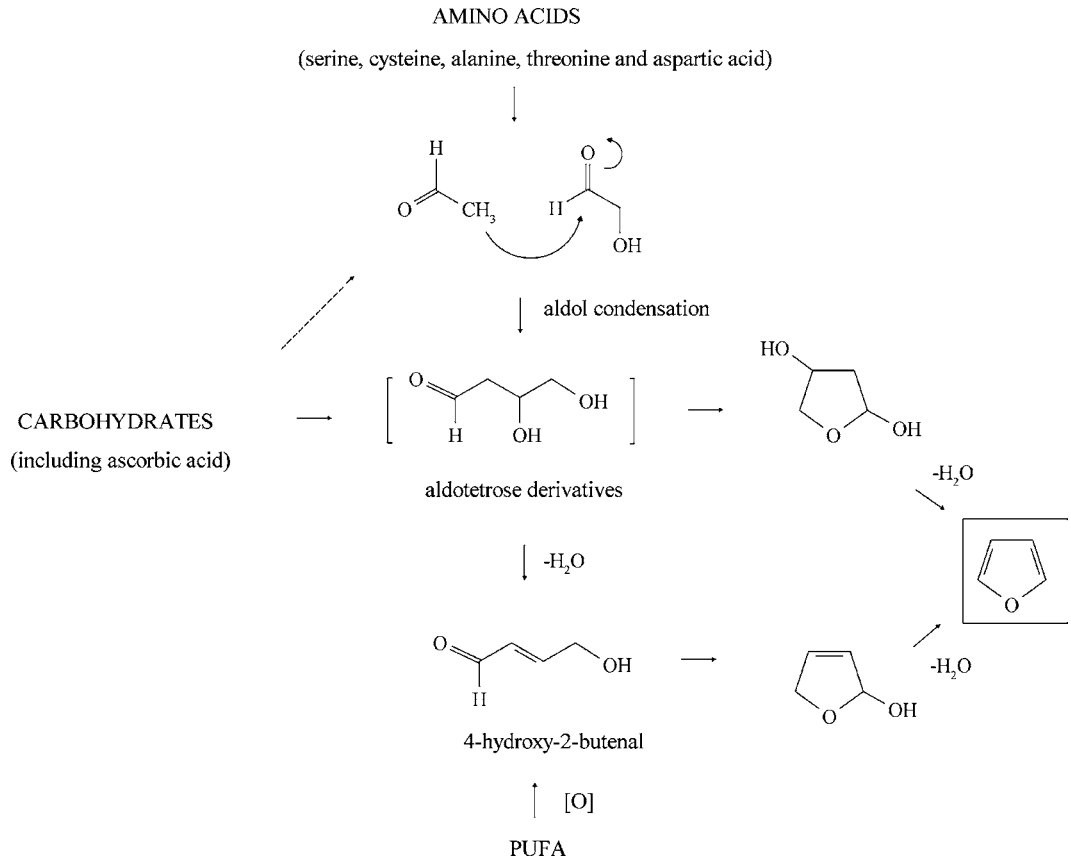

Figure 3. Different origins of the parent furan formation. [O] = oxidation. Dotted arrow indicates minor pathway.

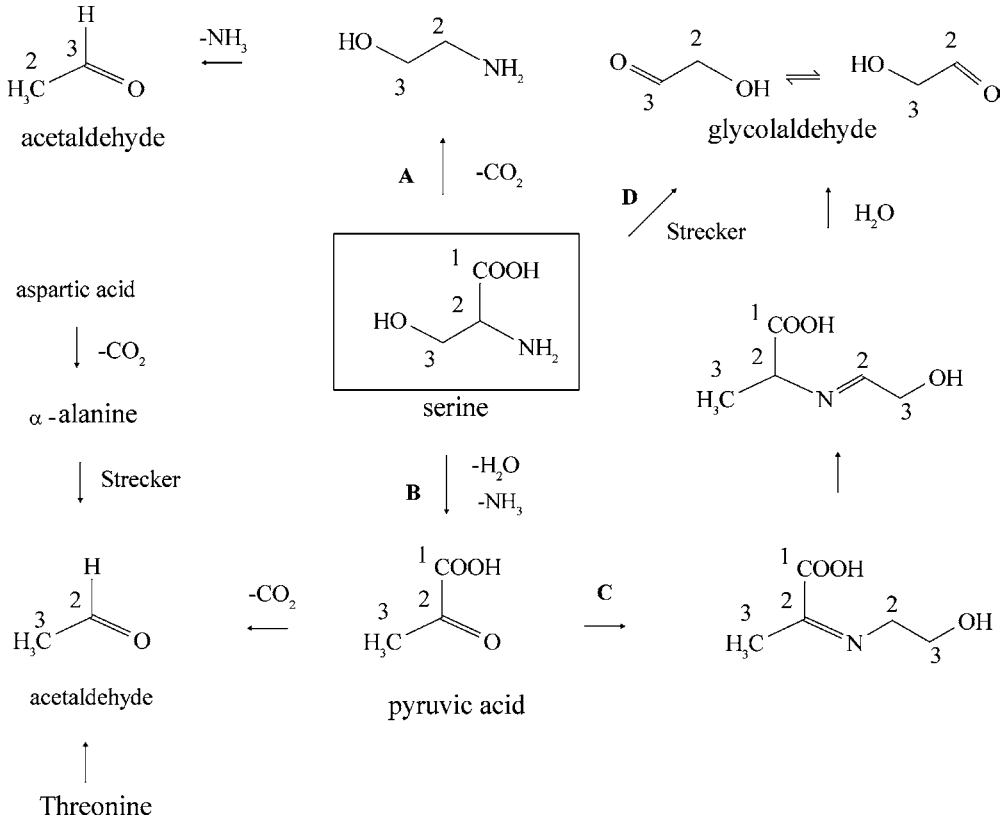

Figure 4. Mechanistic pathways of formation of acetaldehyde and glycolaldehyde (precursors of furan) from different amino acids based on labeling studies. Numbers indicate original amino acid carbon atom locations.

Table 2. Percent Label Distribution in the Parent Furan Generated from Labeled L-Serine

model	M	M + 1	M + 2	M + 3	M + 4
serine	100	0	0	0	0
[1-^{13}C]serine	100	0	0	0	0
[2-^{13}C]serine	0	0	100	0	0
[3-^{13}C]serine	0	0	100	0	0

Table 3. Percent Label Distribution in the Parent Furan Generated from Labeled L-Serine and Unlabeled D-Glucose (3:1 Molar Ratio)

model	M	M + 1	M + 2	M + 3	M + 4
serine	100	0	0	0	0
[1-^{13}C]serine/glucose	100	0	0	0	0
[2-^{13}C]serine/glucose	70	0	30	0	0
[3-^{13}C]serine/glucose	70	0	30	0	0
[2-^{13}C]serine/glucose	80	5	15	0	0
[3-^{13}C]serine/glucose	80	5	15	0	0

(unpublished data). To determine the mechanism of formation of furan from these amino acids, serine independently labeled at C-1, C-2, and C-3 was pyrolyzed and the label incorporation in the parent furan was calculated. The results are given in **Table 2**. According to this table, two of the four carbon atoms of furan originated from C-2 atoms of serine, and the remaining two carbon atoms originated from C-3 atoms of serine. No incorporation of the C-1 atom of serine was detected. These observations are consistent with the proposed aldol condensation mechanism (see **Figure 3**) between an acetaldehyde and a glycolaldehyde moiety originating from serine and eventual formation of furan through an aldotetrose intermediate. Previous studies (*14*, *15*, *17*) have also confirmed the formation of acetaldehyde and glycolaldehyde incorporating the C-2 and C-3 atoms of serine and cysteine, and their mechanism of formation is summarized in **Figure 4**. According to this figure, serine can decarboxylate and produce ethanolamine, which in turn can lose a molecule of ammonia and form acetaldehyde (pathway A). Alternatively, it can undergo dehydration and deamination reactions and form pyruvic acid, which in turn decarboxylates to form acetaldehyde (pathway B). Glycolaldehyde can be formed through the interaction of pyruvic acid with ethanolamine, followed by isomerization of the imine and hydrolysis (pathway C, **Figure 4**). However, in the presence of sugars, it can also be formed through a Strecker reaction (pathway D). Similar pathways can be envisaged for cysteine. Other amino acids that can contribute to the formation of furan are aspartic acid, α-alanine, and threonine; however, these amino acids can generate only acetaldehyde and need reducing sugars to produce glycolaldehyde. The amino acid α-alanine, for example, does not produce furan alone; however, in the presence of glycolaldehyde or a glycolaldehyde source such as glucose, it can generate furan (see **Table 1**). Acetaldehyde can be generated from α-alanine through Strecker reaction, and α-alanine in turn can be generated from aspartic acid through decarboxylation reaction (see **Figure 4**). Threonine, on the other hand, has been shown (*17*) to produce acetaldehyde and hence can generate furan in the presence of sugars as confirmed in **Table 1**.

Furan Formation through Carbohydrate Degradation. To identify possible pathways of formation of furan from carbohydrates, Py-GC-MS analysis of serine/glucose model system was used due to the availability of independently labeled serine and glucose at all of their carbon atom locations (see **Tables 3** and **4**). Inspection of the data in **Table 3** indicated that in the model system where excess labeled serine was reacted with unlabeled glucose, 70% of the furan originated from glucose carbon atoms and 30% from serine carbon atoms. This conclusion was further confirmed when excess unlabeled serine was

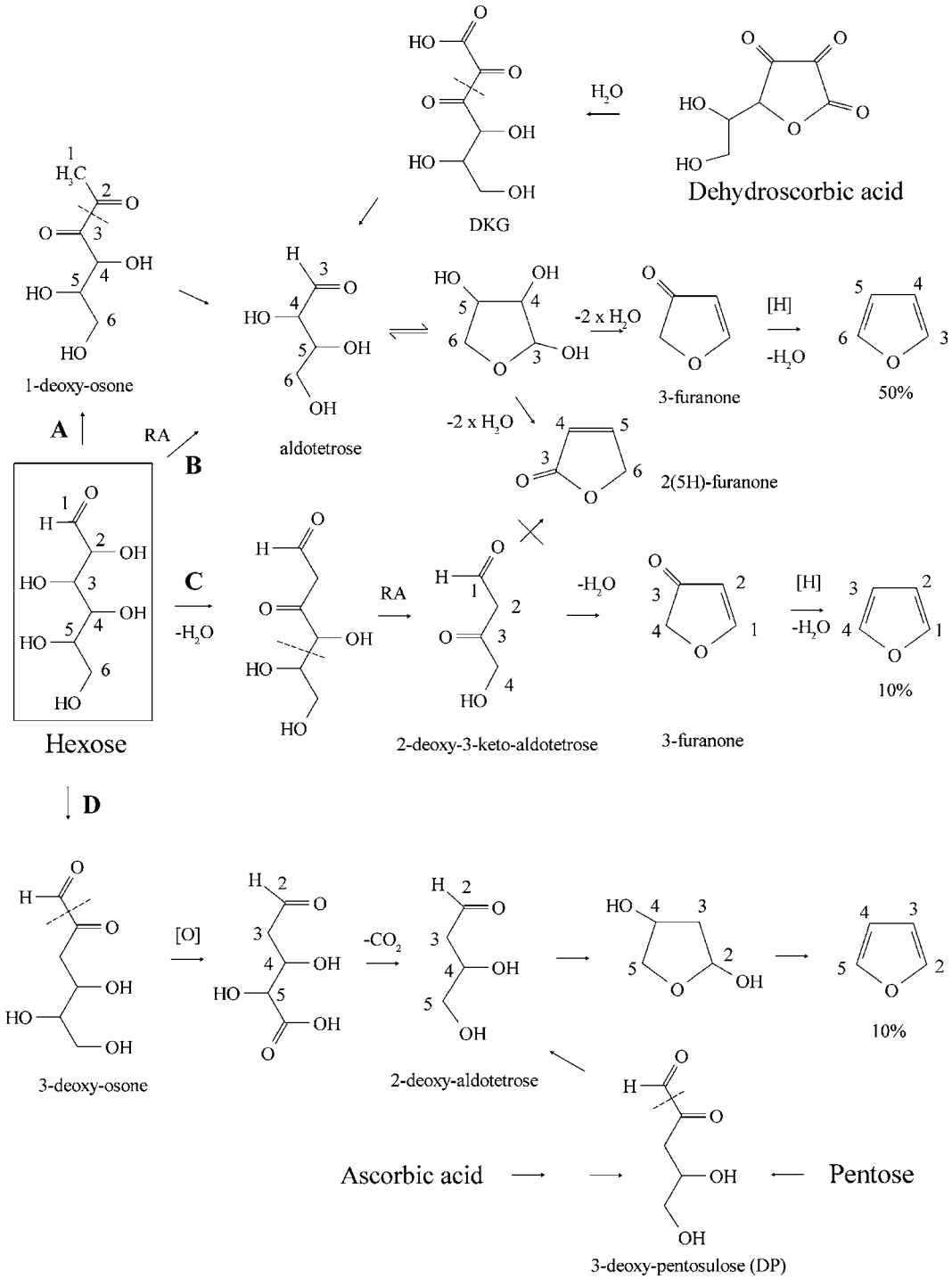

Figure 5. Mechanistic pathways of formation of the parent furan from hexoses, pentoses, and tetroses based on labeling studies. DKG = 2,3-diketogulonic acid; RA = retro-aldol cleavage; [O] = oxidation; [H] = reduction; numbers indicate original D-glucose carbon atom locations. Percent distribution reported takes into consideration the presence of 30% unlabeled furan originating from L-serine.

reacted with [U-^{13}C]glucose (see **Table 4**). Furthermore, inspection of **Table 3** revealed that when glucose was in excess, 5% of the furan formed was singly labeled, indicating a minor contribution of carbohydrate degradations to the $C_2 + C_2$ aldol condensation pathway shown in **Figure 3**. In addition, analysis of the percent label incorporation pattern (**Table 4**) has indicated that there are four pathways (A, B, C, and D in **Figure 5**) of sugar degradation that can lead to the formation of aldotetrose derivatives that can eventually cyclize to form furan as depicted in **Figure 5**. In the glucose/excess serine model system and as indicated above, 30% of the furan originated from serine and the remaining 70% was generated from glucose. The major pathway (50%) of glucose degradation (pathway A or B) that leads to furan formation incorporated the C3−C4−C5−C6 carbon atoms of glucose, 10% incorporated the C1−C2−C3−C4 carbon atoms of glucose (pathway C), and another 10% incorporated the C2−C3−C4−C5 carbon atoms of glucose (pathway D).

Proposed Pathway from Hexose Sugars. Reducing hexoses are known (*18*) to undergo Maillard reaction in the presence of amino acids and generate reactive intermediates such as 1-deoxy- and 3-deoxyosones (pathways A and D) shown in **Figure 5**. These intermediates are also known to be formed in the absence of amino acids (such as pathway B), however, to a

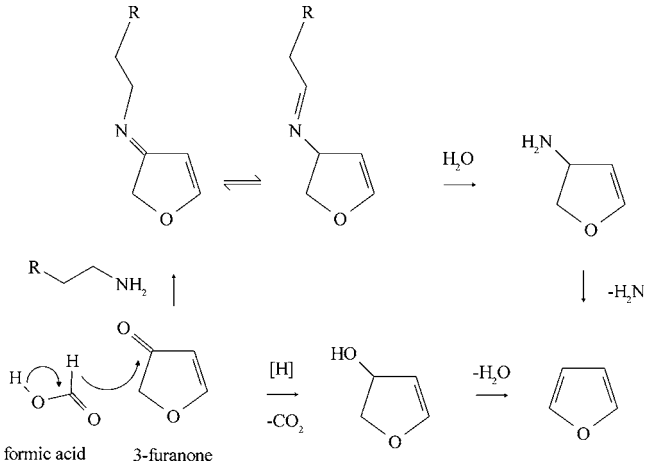

Figure 6. Proposed mechanism of conversion of 3-furanone into furan through reduction and transamination.

lesser extent. The major pathway of furan formation (pathway A) can be initiated by the formation of 1-deoxyosone in the presence of amino acids or through a retro-aldol cleavage (pathway B). Both pathways lead to the formation of an aldotetrose sugar moiety such as erythrose. The 1-deoxyosone, however, needs to undergo α-dicarbonyl cleavage (*18*) to produce the same intermediate. The resulting aldotetrose moiety that contains the C3−C4−C5−C6 carbon atoms of glucose can undergo dehydration reactions and can produce both 3-furanone and 2(5*H*)-furanone. Only the former can be converted into furan through further reduction and dehydration reactions (see **Figure 6**). Reductions in sugar/amino acid mixtures can be effected by formic acid—a major sugar degradation product (*16*)—or through a transamination reaction as shown in **Figure 6**. **Table 1** also indicates that addition of sodium formate to glucose doubles the amount of furan formation, confirming the above hypothesis. The second pathway that incorporates the C1−C2−C3−C4 carbon atoms of glucose into furan can originate from glucose after a dehydration reaction (**Figure 5**, pathway C) followed by a retro-aldol cleavage to form 2-deoxy-3-ketoaldotetrose. The latter intermediate can cyclize after a dehydration step to produce 3-furanone, similar to pathway A or B. The third pathway (**Figure 5**, pathway D) that incorporates the C2−C3−C4−C5 carbon atoms of glucose into furan can arise through α-dicarbonyl cleavage of the 3-deoxyosone intermediate followed by oxidation of the terminal primary hydroxyl group into the carboxylic acid moiety. This intermediate can lose the

Table 4. Percent Label Distribution in the Parent Furan Generated from Unlabeled L-Serine and Labeled D-Glucose (3:1 Molar Ratio)

model	M	M + 1	M + 2	M + 3	M + 4
serine/glucose	100	0	0	0	0
serine/[1-^{13}C]glucose	90	10	0	0	0
serine/[2-^{13}C]glucose	80	20	0	0	0
serine/[3-^{13}C]glucose	30	70	0	0	0
serine/[4-^{13}C]glucose	30	70	0	0	0
serine/[5-^{13}C]glucose	40	60	0	0	0
serine/[6-^{13}C]glucose	50	50	0	0	0
serine/[U-^{13}C]glucose	30	0	0	0	70

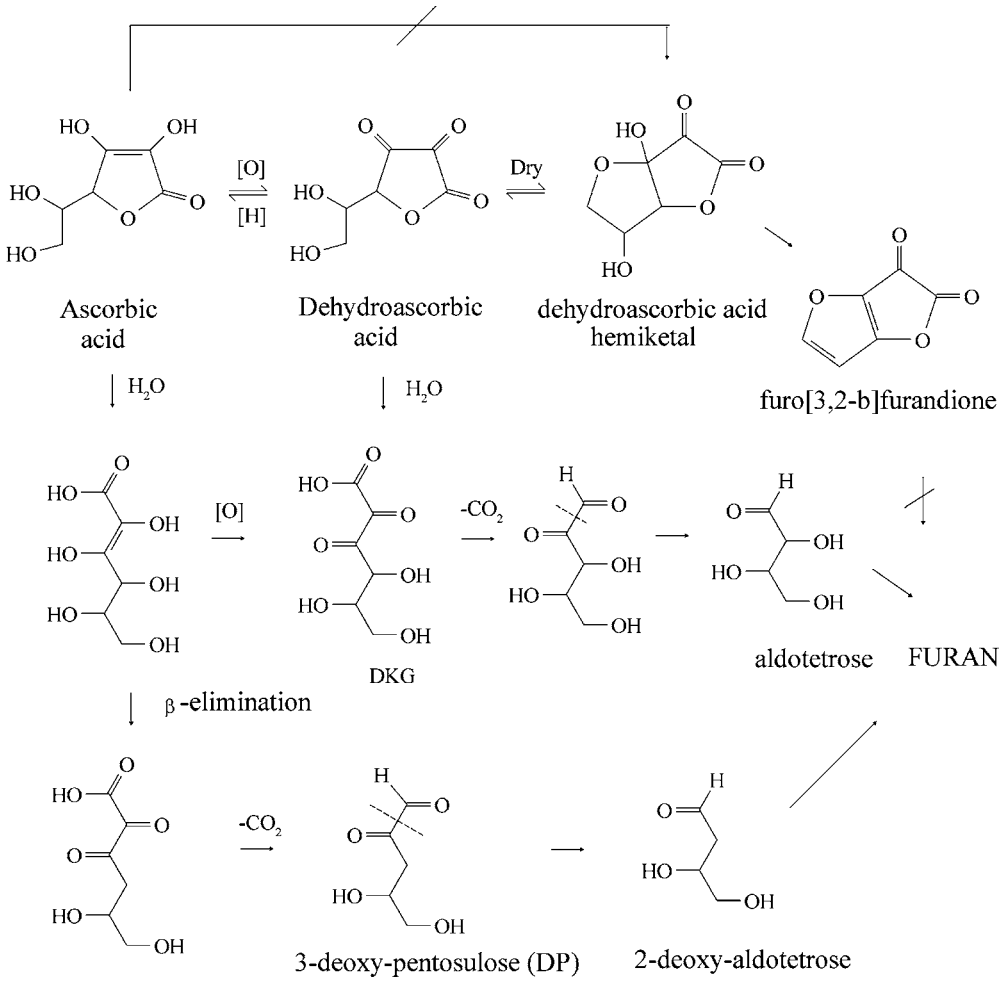

Figure 7. Proposed mechanism of oxidative and nonoxidative degradation of L-ascorbic acid into furan. RA = retro-aldol cleavage; [O] = oxidation; [H] = reduction.

Table 5. Percent Label Distribution in 2(5*H*)-Furanone Generated from Unlabeled L-Serine and Labeled D-Glucose (3:1 Molar Ratio)

model	M	M + 1	M + 2	M + 3	M + 4
serine/glucose	100	0	0	0	0
serine/[1-^{13}C]glucose	100	0	0	0	0
serine/[2-^{13}C]glucose	100	0	0	0	0
serine/[3-^{13}C]glucose	0	100	0	0	0
serine/[4-^{13}C]glucose	0	100	0	0	0
serine/[5-^{13}C]glucose	0	100	0	0	0
serine/[6-^{13}C]glucose	0	100	0	0	0
serine/[U-^{13}C]glucose	0	0	0	0	100

C-6 carbon through decarboxylation to generate 2-deoxyaldotetrose, which can be easily converted into furan as shown in **Figure 5**. The observation that 2(5*H*)-furanone incorporates only the C3−C4−C5−C6 carbon atoms of glucose (see **Table 5**) provides further evidence to the above proposed pathways.

Proposed Pathway from Pentose Sugars. Pentose sugars such as ribose can also generate the parent furan, but more so in the presence of amino acids (see **Table 1**). Similar to hexoses, pentoses can be converted into their 3-deoxyosone derivatives (*18*) either through amino acid reaction or through dehydration at the C-3 hydroxyl group. The resulting intermediate can undergo α-dicarbonyl cleavage to produce 2-deoxyaldotetrose, a direct precursor of furan as shown in **Figure 5**. The increase in the efficiency of ribose or hexose sugars to produce furan in the presence of amino acids can be directly related to their ability to catalyze the formation of deoxyosone derivatives.

Proposed Pathway from Ascorbic Acid. Ascorbic acid is known to oxidize quickly into dehydroascorbic acid and hydrolyze in food systems (*19*, *20*) into 2,3-diketogulonic acid (DKG). A pathway to furan can be envisaged from DKG through α-dicarbonyl cleavage after decarboxylation and generation of the same aldotetrose moiety as hexose sugars (see **Figure 5**). Although, under mainly nonoxidative pyrolytic conditions, ascorbic acid cannot undergo oxidation to produce DKG, instead, it can hydrolyze and undergo β-elimination (*21*) followed by decarboxylation to produce 3-deoxypentosulose (DP) and encounter the ribose pathway of decomposition to generate furan as shown in **Figures 5** and **7**. Unlike the aldotetrose intermediate, the 2-deoxyaldotetrose does not require a reduction step and directly produces the parent furan. Therefore, under nonoxidative conditions, ascorbic acid is a more efficient source of furan than dehydroascorbic acid (see **Table 1**). This order may be reversed under oxidative degradation conditions. Furthermore, under dry-heating conditions, dehydroascorbic acid can cyclize and exist mainly in its hemiketal form, thus preventing the formation of furan as shown in Figure 7. Due to the unavailability of labeled ascorbic acid, we could not confirm the proposed pathways of formation of furan from ascorbic acid as shown in **Figures 5** and **7**. An alternative pathway could be envisaged from aldol condensation of acetaldehyde and glycolaldehyde, similar to the pathway originating from amino acids (see Figure 3). These intermediates are proposed to be formed from the thermal degradation of ascorbic acid at 180 °C (*22*).

LITERATURE CITED

(1) FDA. http://www.fda.gov.

(2) International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Vol. 63: Dry Cleaning, Some Chlorinated Solvents and Other Industrial Chemicals*; Lyon, France, 1995; pp 3194−3407.

(3) Maga, J. A. Furans in foods. *CRC Crit. Rev. Food Sci. Nutr.* **1979**, *11*, 355−400.

(4) Persson, T.; von Sydow, E. Aroma of canned beef: Gas chromatographic and mass spectrometric analysis of the volatiles. *J. Food Sci.* **1973**, *38*, 377−385.

(5) Stoffelsma, J.; Sipma, G.; Kettenes, D. K.; Pypker, J. New volatile components of roasted coffee. *J. Agric. Food Chem.* **1968**, *16*, 1000−1004.

(6) Health Canada. http://www.hc-sc.gc.ca.

(7) Chang, S. S.; Smouse, T. H.; Krishnamurthy, R. G.; Mookherjee, B. D.; Reddy, R. B. Isolation and identification of 2-pentyl-furan as contributing to the reversion flavour of soybean oil. *Chem. Ind. (London)* **1966**, 1926−1927.

(8) Sayre, L. M.; Arora, P. K.; Iyer, R. S.; Salomon, R. G. Pyrrole formation from 4-hydroxynonenal and primary amines. *Chem. Res. Toxicol.* **1993**, *6*, 19−22.

(9) Erdelmeier, I.; Gérard-Monnier, D.; Yadan, J.-C.; Chaudière, J. Reactions of *N*-methyl-2-phenylindole with malondialdehyde and 4-hydroxyalkenals. Mechanistic aspects of the colorimetric assay of lipid peroxidation. *Chem. Res. Toxicol.* **1998**, *11*, 1184−1194.

(10) Vichi, S.; Pizzale, L.; Conte, L. S.; Buxaderas, S.; López-Tamames, E. Solid-phase microextraction in the analysis of virgin olive oil volatile fraction: modifications induced by oxidation and suitable markers of oxidative status. *J. Agric. Food Chem.* **2003**, *51*, 6564−6571.

(11) Xu, G.; Sayer, L. M. Structural characterization of a 4-hydroxy-2-alkenal-derived fluorophore that contributes to lipoperoxidation-dependent protein cross-linking in aging and degenerative disease. *Chem. Res. Toxicol.* **1998**, *11*, 247−251.

(12) Nadkarni, D. V.; Sayre, L. M. Structural definition of early lysine and histidine chemistry of 4-hydroxynonenal. *Chem. Res. Toxicol.* **1995**, *8*, 284−291.

(13) Yaylayan, V. A.; Keyhani. Origin of carbohydrate degradation products in L-alanine/D-[^{13}C]glucose model systems. *J. Agric. Food Chem.* **2000**, *48*, 2415−2419.

(14) Yaylayan, V. A.; Wronowski, A. The influence of pyrolytic and aqueous phase reactions on the mechanism of formation of Maillard products. *J. Agric. Food Chem.* **2000**, *48*, 3549−3554.

(15) Yaylayan, V. A.; Keyhani; Wnorwoski, A. Formation of sugar-specific reactive intermediates from ^{13}C-labeled serines. *J. Agric. Food Chem.* **2000**, *48*, 636−641.

(16) Yaylayan, V. A.; Machiels D.; Istasse, L. Thermal decomposition of specifically phosphorylated D-glucoses and their role in the control of Maillard reaction. *J. Agric. Food Chem.* **2003**, *51*, 3358−3366.

(17) Yaylayan, V.; Wnorowski, A. The role of L-serine and L-threonine in the generation of sugar-specific reactive intermediates during Maillard reaction. In *Food Flavors and Chemistry—Advances of the New Millennium*; Spanier, A., Shahidi, F., Parliment, T., Mussinan, C.; Ho, C.-T., Contis, E., Eds.; Royal Society of Chemistry: Cambridge, U.K., 2001; pp 313−317.

(18) Weenen, H. Reactive intermediates and carbohydrate fragmentation in Maillard chemistry. *Food Chem.* **1998**, *62*, 393−401.

(19) Liao, M.-L.; Seib, P. A. Selected reactions of L-ascorbic acid related to foods. *Food Technol.* **1987**, *41*, 104−107, 111.

(20) Shephard, A. B.; Nichols, S. C.; Braithwaite, A. Moisture induced solid-phase degradation of L-ascorbic acid. Part 1: a kinetic study using tristimulus calorimetry and a quantitative HPLC assay. *Talanta* **1999**, *48*(3), 595−606.

(21) Niemelä, K. Oxidative and non-oxidative alkali-catalysed degradation of L-ascorbic acid. *J. Chromatogr.* **1987**, *399*, 235−243.

(22) Vernin, G.; Chakib, S.; Rogacheva, S.; Obretenov, T. D.; Párkányi, C. Thermal decomposition of ascorbic acid. *Carbohydr. Res.* **1998**, *305*, 1−15.

Received for review June 14, 2004. Revised manuscript received August 27, 2004. Accepted September 5, 2004. We acknowledge funding for this research by the Natural Sciences and Engineering Research Council of Canada (NSERC).

JF0490403